REMARKS

These remarks are in response to the Office Action mailed September 10, 2007. Claims 17, 19, 20 and 30 have been canceled without prejudice to Applicants' prosecuting the canceled subject matter in any divisional, continuation, continuation-in-part or other application. The claims have been amended to set forth proper antecedent basis for various claim terms. No new matter is believed to have been introduced.

I. INTERVIEW SUMMARY

Applicants' thank Examiner Desai for the courteous telephonic interview, which was conducted on October 25, 2007, between the Examiner and Applicants' representative, Joseph Baker.

During the interview the pending rejections were discussed, including suggested claim language, including changes from "moiety" to "domain" and typographical errors in Claim 3. In addition, the pending art rejection was discussed. No agreement was reached and Applicants' representative agreed to submit a formal response.

II. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-4, 6, 11-19, 32 and 33 stand rejected under 35 U.S.C. §112, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Office Action alleges the disclosure does not direct one of ordinary skill in the art to the genus of protein transduction moieties that can be conjugate to

the genus of heterologous polypeptides or a genus of protein transduction moieties that can be conjugated to the genus of fusogenic polypeptides. Applicants respectfully traverse this rejection.

The claims refer to "protein transduction domain" (PTD) to identify a class capable of traversing the cell membrane. This genus is well recognized in the art and includes a number of existing and easily identified species. Thus, Applicants' disclosure reasonably conveys a genus of PTDs known or identifiable in the art.

The claims refer to "fusogenic protein" to identify a class of proteins that facilitates the destabilization of a cell membrane or the membrane of a cell organelle. The Applicants provide a number of fusogenic polypeptides that can be used in the methods and compositions of the invention. For example, the hemagglutinin (HA) of influenza is one example of a fusogenic polypeptide. Other examples, provided by the specification and demonstrated to work include synthetic peptides such as the N-terminus region of the influenza hemagglutinin protein destabilize membranes; HA2 analogs include GLFGAIAGFIEGGWTGMIDG (SEQ ID NO:2); GLFEAIAEFIEGGWEGLIEG (SEQ ID NO:3); the M2 protein of influenza A viruses employed on its own or in combination with the hemagglutinin of influenza virus or with mutants of neuraminidase of influenza A, which lack enzyme activity, but which bring about hemagglutination; peptide analogs of the influenza virus hemagglutinin; the HEF protein of the influenza C virus, the fusion activity of the HEF protein is activated by cleavage of the HEFO into the subunits HEF1 and HEF2; the transmembrane glycoprotein of filoviruses, such as, for example, the Marburg virus, the Ebola virus; the transmembrane glycoprotein of the rabies virus; the transmembrane glycoprotein (G) of the vesicular stomatitis virus; the fusion polypeptide of the Sendai virus, in particular the amino-terminal 33 amino acids of

the F1 component; the transmembrane glycoprotein of the Semliki forest virus, in particular the E1 component, the transmembrane glycoprotein of the tickborn encephalitis virus; the fusion polypeptide of the human respiratory syncytial virus (RSV) (in particular the gp37 component); the fusion polypeptide (S protein) of the hepatitis B virus; the fusion polypeptide of the measles virus; the fusion polypeptide of the Newcastle disease virus; the fusion polypeptide of the visna virus; the fusion polypeptide of murine leukemia virus (in particular p15E); the fusion polypeptide of the HTL virus (in particular gp21); and the fusion polypeptide of the simian immunodeficiency virus (SIV). Methods for isolation/identification of viral fusogenic proteins are obtained either by dissolving the coat proteins of a virus concentration with the aid of detergents (such as, for example, Y-D-octylglucopyranoside) and separation by centrifugation (review in Mannio *et al.*, BioTechniques 6, 682 (1988)) or else with the aid of molecular biology methods known to the person skilled in the art.

Accordingly, the genus of fusogenic moieties is well recognized in the art and includes a number of existing and easily identified species. Thus, Applicants' disclosure reasonably conveys a genus of fusogenic moieties known or identifiable in the art.

For at least the foregoing reasons, Applicants submit that the inventors at the time of filing the application were in possession of the claimed invention as demonstrated by the specification and that the reliance upon Violini *et al.* and Falnes *et al.* for the teaching that the invention was not in Applicants position at the time of filing is in error.

Claims 1-4, 6, 11-19, 32 and 33 stand rejected under 35 U.S.C. §112, first

paragraph, because the specification, while being enabled for the conjugates disclosed in the examples, allegedly does not provide enablement for any conjugates as currently claimed. The specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Applicants respectfully traverse this rejection.

The specification provides sufficient description in view of the skill in the art, to make and use the claimed invention. As described in the specification, any number of molecules have been linked to protein transduction domains. Furthermore, a large number of fusogenic domains are known in the art. Methods of conjugating PTDs, fusogenic and heterologous molecules are known in the art. As additional proof of principle (following Applicants' priority date), please see attached Exhibit C (Michiue *et al.* J. Biol. Chem. 280(9):8285-89, 2005). Michiue et al. demonstrate that a PTD fused to a p53 protein and a fusogenic domain can be useful to treat cancer (see abstract).

III. REJECTION UNDER 35 U.S.C. §102

Claims 31, 34, 35 and 36 stand rejected under 35 U.S.C. §102 as allegedly anticipated by Navarro-Quiroga *et al.* (Molecular Brain Research 105:86-97, 2002). Applicants respectfully traverse this rejection.

Navarro-Quiroga *et al.* teach that an HA2 peptide linked to an NT-polylysine moiety results in neuronal uptake in "NTRH-bearing neurons." (see abstract). The neurotensin (NT) is not a protein transduction domain, but is rather a targeting domain that binds with an NT receptor bearing cell, particularly neuronal cells. Poly-lysine has a cationic character and facilitates interaction with anionically charged

nucleic acids. In fact, Moore *et al.* (J. Biol. Chem. 279(31):32541-32544, 2004) indicate that polylysine reduces uptake and protein transduction (see, *e.g.*, Figure 2). Furthermore, a nuclear localization signal, as described by Navarro-Quiroga *et al.*, is not a protein transduction domain. What Navarro-Quiroga *et al.* describes are targeting moieties (NT and a nuclear localization moiety) linked to a fusogenic domain. Navarro-Quiroga *et al.* do not teach or suggest a fusogenic domain linked to a protein transduction domain as recited in Applicants' claim 31, which are useful for improved cargo delivery and release from macropinosomes. Accordingly, Navarro-Quiroga *et al.* cannot anticipate Applicants' claimed invention.

The Examiner is invited to call the undersigned at 858.509.7300 should any additional issue remain regarding this response.

The Commissioner is hereby authorized to charge any fee deficiency or credit any overpayment of fees to Deposit Account No. 02-4800.

Respectfully submitted,

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Date: October 29, 2007

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